

young and fat patients, owing to the greater richness of the lymphatic supply. Efficient roentgen treatment must take care of these variations.

It is generally conceded that the smaller the caliber of the lymphatics, as well as the greater the degree of semile atrophy, the greater the tendency to oppose cancer dissemination. If the roentgen rays did nothing more to adjacent lymphatics than produce a sclerosis the treatment would still be indicated for retarding the disease. The frequent involvement of one breast to the other is due to the distribution of the lymphatics of the chest wall. Autopsy has shown that the liver metastasizes more frequently than any of the internal organs, and in many cases becomes involved in comparatively early stages.

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**INFLUENCE OF RADIUM WATER THERAPY ON CREATININ  
AND URIC ACID METABOLISM IN CHRONIC  
ARTHRITIS.**

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It seems to be well established that ingestion of water impregnated with radium emanation is highly effective in the treatment of certain forms of chronic arthritis. An analysis of 471 cases of chronic arthritis under radium therapy reported by thirteen authors showed definite improvement in 391 cases, of which 102 were practically cured.<sup>1</sup> Out of 165 cases of gout all but 16 showed improvement, but despite numerous studies we do not yet understand the *rationale* of the radium therapy.

The special effectiveness of radium therapy in gout directed early attention to the influence of radium on the uric acid metabolism. As a result of the investigations in His's clinic, it was affirmed that uric acid occurs in the blood in gout in a specially insoluble modification and that under the influence of radium this insoluble pathological form of uric acid becomes changed to the more soluble physiological form, which is easily destroyed and excreted, the net result being a rapid solution of the gouty tophi,

<sup>1</sup> Rowntree, L. G., and Baetger, W. A.: Radium in Internal Medicine: its Pathological and Pharmacological Effects, Jour. Am. Med. Assn., 1913, ii, 1438.

an increased elimination of uric acid in the urine and a disappearance of uric acid from the blood.<sup>2</sup>

The experiments on which these investigators based their theory of gout and the action of radium were at first apparently confirmed.<sup>3</sup> But more carefully controlled observations, with reliable methods, have failed to confirm them. Radium does not appear to influence the rate of uric acid decomposition,<sup>4</sup> the solubility of uric acid,<sup>5</sup> the uric acid content of the blood<sup>6</sup> or the rate of uric acid excretion.<sup>7</sup> Further study of the subject seems therefore desirable.

At the Robert B. Brigham Hospital we have had an opportunity to study the influence of radium on the metabolism of three patients with chronic arthropathies: A man, aged eighteen years, with the

<sup>2</sup> Gudzent, F.: Physikalisch-Chemisches Verhalten der Harnsäure und ihre Salze im Blut, *Ztschr. f. physiol. Chem.*, 1909, Ixiii, 455. Gudzent, F.: Der Einfluss von Radium auf die harnsäuren Salze, *Deutsch. med. Wehnschr.*, 1909, No. 35, i, 920. Gudzent, F., und Loewenthal: Ueber den Einfluss der Radiumemanation auf den Purinstoffwechsel, *Ztschr. f. klin. Med.*, 1910, Ixii, 304. Gudzent, F.: Einiges über die biologischen Eigenschaften der Radiumemanation und ihre Anwendung bei Krankheiten, Radium in Biologie und Heilkunde, 1911, i, 14. Gudzent, F.: Klinische Erfahrungen über die Behandlung der Arthritiden und der Gicht mit Radiumemanation, Radium in Biologie und Heilkunde, 1911, i, 132. Gudzent, F.: Klinische Erfahrungen über die Behandlung der Arthritiden und der Gicht mit Radiumemanation, *Berl. klin. Wehnschr.*, 1911, xviii, 2098. His, W.: Die Behandlung der Gicht und des Rheumatismus mit Radium, *Berl. klin. Wehnschr.*, 1911, xviii, 197.

<sup>3</sup> Uric Acid Destruction by Radium. Mesernitsky, P.: Die Zersetzung von Oxyurinen durch Radiumemanation, *Zentralbl. f. inn. Med.*, 1912, p. 573. Diminution or Disappearance of Blood Uric Acid under Radium. Mesernitsky, P.: Ueber die Schädigung des Organismus durch hohe Dosen von Radiumemanation, *Arch. f. physikal. Med.*, 1911-12, vi, 50. Falta, W., und Zehner, L.: Ein Fall von Gicht mit Thorium-X behandelt, *Wien. klin. Wehnschr.*, 1912, No. 25, ii, 1969. Increased Uric Acid Excretion after Radium. Mesernitsky, P., und Kemen, J.: Ueber Purinstoffwechsel bei Gichtkranken unter Radiumemanation-behandlung, Therapie der Gegenwart, 1910, N. F., xii, 526. Armstrong: Die Radiumbehandlung von Stoffwechselkrankheiten, 28 Kongr. f. inn. Med., 1911, p. 148. Von Noorden, C. und Falta, W.: Klinische Beobachtungen über die physiologische und therapeutische Wirkung grosser Dosen von Radiumemanation, *Med. Klinik*, 1911, No. 7, ii, 1487. Kikkoi, T.: Ueber den Einfluss von Radiumemanation auf den Stoffwechsel im Organismus, Radium in Biologie und Heilkunde, 1911, i, 46. Mesernitsky, P.: Ueber die Schädigung des Organismus durch hohe Dosen von Radiumemanation, *Arch. f. physikal. Med.*, 1911-12, vi, 50.

<sup>4</sup> Knuff-Lenz, E. von, und Wieschowski, W.: Ueber die Wirkung von Radiumemanation auf Mononatriumurat, *Ztschr. f. physiol. Chem.*, 1912, lxxvii, 303.

<sup>5</sup> Kerb, J., und Lazarus, P.: Zur Frage des Abbaues von Mononatriumurat unter dem Einfluss von Radiumemanation bzw. Radium D, *Biochem. Ztschr.*, 1912, xlii, 82.

<sup>6</sup> Chase, A. F., and Fine, M. S.: The Use of Atophan and Radium Emanation in the Treatment of Gout and Arthritides, *Jour. Am. Med. Assn.*, 1914, Ixii, 945. Fine and Chase: *Jour. Pharm. and Exp. Therap.*, 1914, vi, 219.

<sup>7</sup> Mannes und Wellman: Klinische Erfahrungen in der Behandlung mit Radium Trink und Badekuren, *Ztschr. f. physik. und. Diät. Therapie*, 1910, xiv, 321. Umber in the discussion of Armstrong's paper: Die Radiumbehandlung von Stoffwechselkrankheiten, Verhandl. de Kongr. f. inn. Med., 1911, 28, 48, see p. 177. Mandel, H.: Arthritis urica unter Radiumemanation, Radium in Biologie und Heilkunde, 1911, ii, 162. Kehler: Neue Beobachtungen über die Wirkungsweise von Atophan und Radium im Purinstoffwechsel und deren Bedeutung f. Pathogenese, Diagnose, und Therapie der Gicht, *Arch. f. Verdauungskrank.*, 1913, 19. Ergangzungsheft, p. 98. Rosenblom, F.: A Study of the Urinary Nitrogen and Sulphur Partition in a Case of Rheumatoid Arthritis Treated with Intravenous Injection of Radium Salts, *Am. Jour. Med. Sc.*, 1915, xlvii, 718.

infectious type; a woman, aged sixty-one years, with the hypertrophic type; a woman, aged sixty-five years, with the gouty type.<sup>8</sup>

These patients, who were on a purin-free, creatin-free diet, received, five times a day, 3 ounces of water impregnated with radium emanations, 20,000 Maché units in all. We measured the daily urinary output of uric acid, creatinin, nitrogen and water and the uric acid content of the blood before, during and after the treatment.<sup>9</sup>

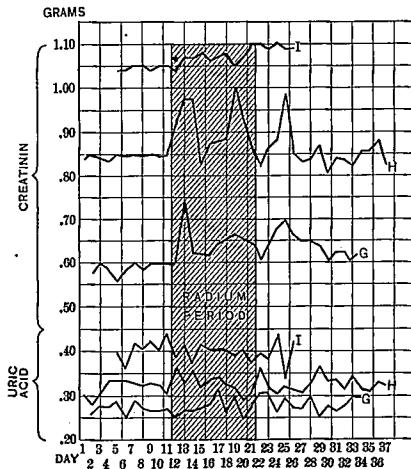
Day.	Hypertrophic arthritis.		Gout.		Chronic arthritis, infectious type.	
	Creatinin.	Uric acid.	Creatinin.	Uric acid.	Creatinin.	Uric acid.
Preliminary period.						
1	0.839	0.308	0.577	0.262		
2	0.836	0.316	0.611	0.280		
3	0.847	0.307	0.588	0.277		
4	0.833	0.339	0.559	0.287		
5	0.849	0.335	0.559	0.287		
6	0.844	0.335	0.585	0.251		
7	0.845	0.330	0.597	0.291	1.04	0.400
8	0.840	0.322	0.684	0.274	1.04	0.357
9	0.846	0.328	0.676	0.275	1.05	0.416
10	0.847	0.324	0.594	0.285	1.04	0.422
11	0.843	0.300	0.596	0.272	1.05	0.402
Ave.	0.845 ± 0.003	0.320 ± 0.014	0.523 ± 0.016	0.266 ± 0.016	1.045 ± 0.005	0.401 ± 0.015
Radium period.						
12	0.930	0.362	0.606	0.252	1.05	0.441
13	0.977	0.324	0.740	0.270	1.04	0.386
14	0.975	0.356	0.621	0.269	1.07	0.419
15	0.824	0.320	0.617	0.272	1.07	0.374
16	0.872	0.338	0.617	0.280	1.08	0.414
17	0.861	0.311	0.645	0.243	1.05	0.404
18	0.881	0.324	0.651	0.262	1.07	0.400
19	0.909	0.318	0.684	0.296	1.08	0.400
20	0.929	0.291	0.655	0.245	1.05	0.399
21	0.861	0.310	0.648	0.279	1.07	0.403
Ave.	0.923 ± 0.049	0.328 ± 0.017	0.640 ± 0.025	0.274 ± 0.015	1.10	0.376
After period.						
22	0.822	0.363	0.609	0.308	1.10	0.380
23	0.802	0.318	0.647	0.313	1.09	0.335
24	0.803	0.363	0.630	0.314	1.09	0.424
25	0.835	0.324	0.697	0.242	1.076 ± 0.016 (Ave.)	0.400 ± 0.019 (Ave.)
26	0.851	0.318	0.692	0.277		
27	0.833	0.309	0.649	0.270		
28	0.836	0.331	0.650	0.269		
29	0.870	0.366	0.638	0.250		
30	0.803	0.334	0.606	0.277		
31	0.849	0.337	0.622	0.270		
32	0.837	0.310	0.611	0.274		
33	0.827	0.345	0.606	0.269		
34	0.858	0.318	0.620	0.293		
35	0.859	0.310				
36	0.880	0.332				
37	0.822	0.328				

Only one definite change in the metabolism was observed: A slight increase in the rate of creatinin excretion with a somewhat increased variation in the day-to-day values, an effect which per-

\* The clinical results of our studies of radium therapy are to be published separately.

<sup>9</sup> Creatinin and uric acid analyses were made in duplicate by Folin's colorimetric methods.

sisted for a time after discontinuing the radium treatment. These changes, though slight, are, it will be noticed by comparison with the preliminary periods in each case, outside the limits of variation due to the analysis or to physiological variations. Objective evidence that improper collection of twenty-four-hour specimens is not responsible for the variation is afforded by the fact that the irregularities begin promptly with the radium treatment and are not, moreover, accompanied by similar variations in the uric acid excretion.



The above chart shows the daily excretion of uric acid and creatinin on three patients with chronic arthritis (*I*, infectious type; *H*, hypertrophic type; *G*, gouty type) for a period of thirty-seven days. From the twelfth to the twenty-first day radium water was administered.

The radium therapy had no influence on the uric acid content of the blood or on the rate of excretion of uric acid, total nitrogen or water.

We know, as yet, so little regarding the physiology of creatinin that a full interpretation of the increased creatinin elimination is not possible, but the data would appear to establish the physiological activity of radium water and to raise a considerable doubt that it has any influence on uric acid metabolism.